

CLAIMS

1. A method for delivering a therapeutic dose of a gene expression cassette in a fluid selectively to heart for sustained expression comprising steps of:
 - (a) increasing dwell time of fluid in a targeted area,
 - (b) administration of a vascular permeablizing agent, and
 - (c) administration of a viral vector containing a gene expression cassette of interest.
2. A method as in claim 1, wherein the dwell time is increased by the induction of hypothermia.
3. A method as in claim 1, wherein the dwell time is increased by isolation of the heart from systemic circulation.
4. A method as in claim 1, wherein the dwell time is increased by induction of hypothermia and isolation of the heart from systemic circulation.
5. A method as in claim 1, wherein dwell time is increased by induction of complete or near-complete transient cardiac arrest.
6. A method as in claim 1, wherein dwell time is increased by induction of reversible bradycardia.
7. A method as in claim 1, wherein the vascular permeablizing agent is histamine, substance P or serotonin.
8. A method as in claim 1, wherein at least one bolus of virus is administered.
9. A method as in claim 1, wherein the viral vector is an adenoviral vector.
10. A method as in claim 9, wherein the adenoviral vector contains a strong promoter.

11. A method as in claim 10, wherein the strong promoter is a cytomegalovirus (CMV) promoter.

12. A method as in claim 10, wherein the strong promoter is a Rous sarcoma virus (RSV) promoter.

13. A method as in claim 9, wherein the adenoviral vector contains enhancer elements.

14. A method as in claim 13, wherein the enhancer is a cytomegalovirus (CMV) enhancer.

15. A method as in claim 13, wherein the enhancer is a Rous sarcoma virus (RSV) enhancer.

16. A method as in claim 1, wherein the viral vector is an adenovirus-associated viral (AAV) vector.

17. A method as in claim 16, wherein the AAV vector contains a strong promoter.

18. A method as in claim 17, wherein the strong promoter is a cytomegalovirus (CMV) promoter.

19. A method as in claim 16, wherein the strong promoter is a Rous sarcoma virus (RSV) promoter.

20. A method as in claim 9, wherein the AAV vector contains enhancer elements.

21. A method as in claim 20, wherein the enhancer is a cytomegalovirus (CMV) enhancer.

22. A method as in claim 20, wherein the enhancer is a Rous sarcoma virus (RSV) enhancer.

23. A method as in claim 1, wherein the gene of interest is a structural gene.
24. A method as in claim 23, wherein the structural gene is α -sarcoglycan.
25. A method as in claim 23, wherein the structural gene is β -sarcoglycan.
26. A method as in claim 23, wherein the structural gene is γ -sarcoglycan.
27. A method as in claim 23, wherein the structural gene is δ -sarcoglycan.
28. A method as in claim 1, wherein the gene of interest is a functional gene.
29. A method as in claim 28, wherein the functional gene is β -adrenergic receptor (β -AR).
30. A method as in claim 28, wherein the functional gene is sarcoplasmic reticulum Ca^{2+} ATPase (SERCA-2).
31. A method as in claim 1, wherein the gene of interest is a gene fragment.
32. A method as in claim 1, wherein the gene of interest is a mutated form of a gene.
33. A method as in claim 32, wherein the mutated form of the gene is a dominant negative form of phospholamban (PLB).
34. A method as in claim 32, wherein the SERCA-2 gene is administered in conjunction with a dominant negative form of PLB.
35. A method as in claim 33, wherein the dominant negative form of PLB contains a mutation at amino acid 2 from glutamic acid (E) to alanine (A).

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36. A method as in claim 33, wherein the dominant negative form of PLB contains a mutation at amino acid 14 from arginine (R) to glutamic acid (E).

37. A method as in claim 33, wherein the dominant negative form of PLB contains a mutation at amino acid 16 from serine (S) to asparagine (N).

38. A method as in claim 33, wherein the dominant negative form of PLB contains mutations at amino acid 16 from serine (S) to glutamic acid (E).

39. A method as in claim 33, wherein the dominant negative form of PLB contains a mutation at amino acid 49 from valine (V) to alanine (A).

40. A method as in claim 33, wherein the dominant negative form of PLB contains mutations at amino acid 3 from lysine (K) to glutamic acid (E) and at amino acid 14 from arginine (R) to glutamic acid (E).